

In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS

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LISA MATHIS,

Petitioner,

v.

SECRETARY OF HEALTH
AND HUMAN SERVICES,

Respondent.

* * * * *

Ronald C. Homer & Meredith Daniels, Conway Homer, P.C., Boston, MA, for
petitioner;

Nina Ren, United States Dep't of Justice, Washington, DC, for respondent.

DECISION DENYING ENTITLEMENT¹

Lisa Mathis alleges that an influenza (“flu”) vaccine significantly aggravated her multiple sclerosis (sometimes abbreviated “MS”). Amended Petition, filed April 14, 2021. Ms. Mathis supported her claim with reports from an expert. The Secretary contested Ms. Mathis’s allegations based upon reports from a different expert. Because her expert has not presented a reliable theory to explain how a flu vaccination can worsen multiple sclerosis, Ms. Mathis is not entitled to compensation.

¹ Because this Decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at <https://www.govinfo.gov/app/collection/uscourts/national/cofc>, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the Decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), the parties have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. Any changes will appear in the document posted on the website.

I. **Facts**²

A. **Pre-Vaccination**

Ms. Mathis was born in 1968. Exhibit 1 at 1. In 2018, at the time of her vaccination, she worked for Carpet Bonanza. Exhibit 15 (damages affidavit) ¶ 5.

In the three years before the vaccination, Ms. Mathis sought chiropractic care for problems such as tightness and tingling. Exhibit 6, *passim*. For example, on June 7, 2017, Ms. Mathis reported “intermittent numbing discomfort” in the bottom of her right and left feet. Exhibit 6 at 36. Roughly 16 months later in the final chiropractic appointment before the allegedly harmful vaccination, Ms. Mathis reported intermittent tightness, level five, in the back of her neck and in her low back. *Id.* at 96.

Notably, before the vaccination, no treating doctor diagnosed Ms. Mathis with multiple sclerosis. However, the experts agreed that Ms. Mathis most likely had developed lesions within her central nervous system before the vaccination. Exhibit 17 at 9, Exhibit A at 7; *see also* Pet’r’s Br. at 17. Thus, Ms. Mathis asserts that the flu vaccine significantly aggravated an underlying, but undiagnosed, multiple sclerosis.³

B. **Vaccination and Thereafter**

Ms. Mathis received the flu vaccination on October 25, 2018. Exhibit 1 at 2-4. She was fifty years old.

² As noted in a March 24, 2021 order for briefs, the parties agree that the medical records accurately set forth information about Ms. Mathis’s health around the time the medical record was created. Furthermore, because the outcome of Ms. Mathis’s case does not depend on her health history, this decision’s recitation of facts is abbreviated. For a more detailed description of the events in Ms. Mathis’s life, *see* Pet’r’s Br., filed December 21, 2021, at 2-11 and Resp’t’s Br., filed March 24, 2022 at 5-20.

³ While the experts have determined the lesions revealed on the MRI were old enough that they existed before the vaccination, the experts differ as to whether Ms. Mathis presented any symptom of multiple sclerosis before the vaccination. For Dr. Chwalisz, Ms. Mathis’s symptoms were locatable to peripheral nerves or peripheral nerve roots. Exhibit 17 at 10. In contrast, Dr. Leist stated: “Ms. Mathis had symptoms and exam findings that suggested involvement of the central nervous system well before October 25, 2018.” Exhibit A at 8. Resolving this dispute is not necessary.

In November 2018, Ms. Mathis saw her chiropractor four times and reported problems such as tightness, numbness, tingling and hypertonicity. Exhibit 6 at 100-09. In the November 13 appointment, the chiropractor recommended that Ms. Mathis seek attention from a medical doctor. Id. at 106.

Ms. Mathis informed a colleague of her primary care doctor that she was having constant numbness and tingling on her left side starting after a flu vaccination. Exhibit 2 at 73-79 (November 15, 2018). The doctor ordered an MRI. Id. at 78.

The MRI, which was done on December 4, 2018, showed at least ten lesions in Ms. Mathis's brain. Exhibit 2 at 144. The interpreter indicated that multiple sclerosis should be considered.

A neurologist, Christina Johnson, reviewed the MRI as part of an appointment on January 10, 2019. Exhibit 2 at 154. Dr. Johnson stated the MRI "findings meet clinical criteria for diagnosis of relapsing remitting MS." After additional testing, Dr. Johnson confirmed that Ms. Mathis was suffering from multiple sclerosis. Exhibit 11 at 8-9.

Multiple sclerosis is a demyelinating disease of the central nervous system. Exhibit 17 at 4. According to Ms. Mathis's expert, the "ultimate cause of MS has not been completely established, but it is generally considered an autoimmune disease, related to 'overactivity' of the immune system." Id. at 5. "Initially, most MS patients experience relapses (recurrent episodes of neurologic disease) but eventually in many of the cases the course of the disease becomes chronic and progressive with time." Id.

The remaining medical records do not meaningfully affect whether Ms. Mathis is entitled to compensation. Therefore, although these records have been reviewed, they are not set forth in this decision.

II. Procedural History

The course of litigation was relatively routine. Ms. Mathis initiated this case by filing her petition on April 14, 2020. She alleged the flu vaccine caused her to suffer a demyelinating disorder in her central nervous system. Pet. at 1 (Introduction). She submitted medical records on various dates.

To assist with the presentation of reports from experts, a set of instructions was proposed in draft form on September 10, 2020. After neither party objected to the proposed instructions, they became final pursuant to an October 14, 2020 order.

The Secretary reviewed the evidence Ms. Mathis had submitted and recommended that compensation be denied. Resp't's Rep., filed Nov. 17, 2020. The Secretary maintained that Ms. Mathis suffered from multiple sclerosis before the vaccination. Id. at 6. This assertion was discussed in a December 10, 2020 status conference.

On April 14, 2021, Ms. Mathis amended her petition to present the cause of action on which she is proceeding: the flu vaccination significantly aggravated her multiple sclerosis. The allegations in the amended petition conform to the opinion of an expert whom Ms. Mathis retained, Bart Chwalisz.⁴ Dr. Chwalisz recognized that "Ms. Mathis may have had some clinically silent MS plaques before the vaccine was given but the actual clinical onset of her symptoms clearly dates to the time when she received the influenza vaccine." Exhibit 17 (report) at 10. Dr. Chwalisz also proposed various mechanisms by which a flu vaccine could cause (or aggravate) multiple sclerosis.

The Secretary responded with a report from an expert whom he retained, Thomas Leist.⁵ Dr. Leist opined, "Ms. Mathis had experienced symptoms consistent with prodromal MS for 18 months or longer prior to the inoculation with influenza vaccine on October 25, 2018." Exhibit A (report) at 7. Dr. Leist stated that the flu vaccine "is not known to cause or aggravate MS." Id. at 5. Later, Dr. Leist presented an opinion that Ms. Mathis's symptoms of multiple sclerosis before the vaccination were similar to her symptoms after the vaccination. Exhibit C at 2.

Ms. Mathis declined to submit a report responsive to any opinions Dr. Leist offered. Pet'r's Status Rep., filed Aug. 16, 2021. Thus, because the evidence was complete, the case advanced to the stage in which the parties filed briefs. See Order, issued Aug. 26, 2021.

Ms. Mathis argued that she was entitled to compensation in a 57-page brief filed December 21, 2021. The Secretary challenged Ms. Mathis's position through his brief, which was filed on March 24, 2022 and is 45 pages. With this material, the Secretary submitted a new report from Dr. Leist. Dr. Leist discussed Ms. Mathis's symptoms, which Dr. Leist categorized as spasticity and tonic.

⁴ Dr. Chwalisz earned a medical degree from the University of Chicago in 2011. Exhibit 18 (curriculum vitae). He received additional training in neurology and became board-certified in neurology in 2015. Id. at 8.

⁵ Dr. Leist earned his medical degree from the University of Miami in 1993. Exhibit D (updated curriculum vitae) at 1. He is board-certified in neurology. Id.

Exhibit E. The Secretary contested whether Ms. Mathis had met her burden with respect to a theory by which a flu vaccination might aggravate multiple sclerosis. Resp't's Br. at 30-36.

Ms. Mathis replied, making two primary arguments. First, she argued that Dr. Leist's latest report should be stricken because Dr. Leist had not previously disclosed this opinion. Pet'r's Reply, filed July 11, 2022, at 3. Second, she maintained that she fulfilled her burden to show that she experienced worsened symptoms after the vaccination. *Id.* at 8-14. Ms. Mathis did not address the Secretary's arguments regarding the theories by which the flu vaccine might aggravate multiple sclerosis.

With respect to the question of any pre-vaccination spasticity, the Secretary defended Dr. Leist's new report. Resp't's Resp., filed Aug. 10, 2022. Ms. Mathis also presented a report from Dr. Chwalisz on February 22, 2023. Exhibit 52. The report from Dr. Chwalisz closes the record, making the case ready for resolution.

To adjudicate Ms. Mathis's case, a hearing is not needed. Special masters possess discretion to decide whether an evidentiary hearing will be held. 42 U.S.C. § 300aa-12(d)(3)(B)(v) (promulgated as Vaccine Rule 8(c) & (d)), which was cited by the Federal Circuit in *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1365 (Fed. Cir. 2018). "A special master is not obliged to hold an evidentiary hearing." *Oliver v. Sec'y of Health & Hum. Servs.*, 133 Fed. Cl. 341, 354 (2017), *aff'd*, 900 F.3d 1357, 1363 (Fed. Cir. 2018).

The parties were informed that the case could be decided without a hearing. Order, issued August 26, 2021. Ms. Mathis did not raise any objections to resolving the case without oral testimony. The Secretary encouraged this method of resolution.

Both Dr. Chwalisz and Dr. Leist have previously testified before the undersigned. The undersigned is also familiar with the issues in Ms. Mathis's case. This background assists in the process for resolving this case. See *Whitcotton v. Sec'y of Health & Hum. Servs.*, 81 F.3d 1099, 1104 (Fed. Cir. 1996) (allowing special masters to use their accumulated expertise).

III. Standards for Adjudication

A petitioner is required to establish her case by a preponderance of the evidence. 42 U.S.C. § 300aa-13(1)(a). The preponderance of the evidence standard requires a "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has

the burden to persuade the judge of the fact's existence.” Moberly v. Sec’y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. Bunting v. Sec’y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between “preponderant evidence” and “medical certainty” is important because a special master should not impose an evidentiary burden that is too high. Andreu v. Sec’y of Health & Hum. Servs., 569 F.3d 1367, 1379-80 (Fed. Cir. 2009) (reversing special master’s decision that petitioners were not entitled to compensation); see also Lampe v. Sec’y of Health & Hum. Servs., 219 F.3d 1357 (Fed. Cir. 2000); Hodges v. Sec’y of Health & Hum. Servs., 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with dissenting judge’s contention that the special master confused preponderance of the evidence with medical certainty).

As confirmed in W.C. v. Sec’y of Health & Hum. Servs., 704 F.3d 1352, 1357 (Fed. Cir. 2013), the elements of an off-Table significant aggravation case were stated in Loving. There, the Court blended the test from Althen v. Sec’y of Health & Hum. Servs., 418 F.3d 1274, 1279 (Fed. Cir. 2005), which defines off-Table causation cases, with a test from Whitcotton v. Sec’y of Health & Hum. Servs., 81 F.3d 1099, 1107 (Fed. Cir. 1996), which concerns on-Table significant aggravation cases. The resulting test has six components. These are:

(1) the person’s condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person’s current condition constitutes a “significant aggravation” of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144.

In resolving claims of significant aggravation, special masters may focus their analysis on the last three prongs of the Loving test, which correspond to the traditional Althen factors. Walker v. Sec’y of Health & Hum. Servs., No. 18-299V, 2022 WL 11141194, at *3 (Fed. Cl. Spec. Mstr. Sep. 27, 2022) (citing Hennessey v. Sec’y of Health & Hum. Servs., No. 01-190V, 2009 WL 1709053, at *42 (Fed. Cl. Spec. Mstr. May 29, 2009), mot. for rev. denied, 91 Fed. Cl. 126 (2010)).

IV. Analysis - Medical Theory

Ms. Mathis's claim falters on the fourth Loving prong, which corresponds to the first Althen prong. This prong requires a petitioner to present a theory explaining how a vaccine can harm a recipient.

To support her theory about how a flu vaccine can worsen multiple sclerosis, Ms. Mathis presents two types of arguments. First, she brings forward arguments that, according to her, support the contention that vaccines can worsen multiple sclerosis generally. Second, Ms. Mathis defends the three specific theories about which Dr. Chwalisz opined. These are taken up in turn.

A. **General Propositions**

Ms. Mathis raises two ideas that, if accepted, could enhance the theories explaining how a vaccine might worsen multiple sclerosis. These ideas are (1) the relationship between infections and vaccinations and (2) epidemiology.

1. Infections and Vaccinations

Ms. Mathis presents a syllogism. First, she maintains that flu infections can cause multiple sclerosis to relapse or to flare. Next, she asserts that vaccinations are similar to infections. Therefore, she concludes that vaccinations can also cause multiple sclerosis to relapse or to flare. Pet'r's Br. at 25-27.

Ms. Mathis has not persuasively shown that flu infections are sufficiently similar to flu vaccinations. An infection with the influenza virus leads to replication of the virus within the infected person. In contrast, a flu vaccination does not replicate or expand inside the body. Accordingly, cases have rejected petitioners' attempts to liken the consequences of a non-live vaccination to the consequences of an infection. See Langland v. Sec'y of Health & Hum. Servs., 109 Fed. Cl. 421, 440-42 (2013); Sokol v. Sec'y of Health & Hum. Servs., No. 16-1631V, 2020 WL 553842, at *6 (Fed. Cl. Spec. Mstr. Jan. 9, 2020); Bantugan v. Sec'y of Health & Hum. Servs., No. 15-721V, 2019 WL 7602581, at *18-19 (Fed. Cl. Spec. Mstr. Dec. 20, 2019).

2. Epidemiology

As a second method to shore up the theories by which a flu vaccine might significantly aggravate multiple sclerosis, Ms. Mathis cites three epidemiologic studies. Pet'r's Br. at 27-29. The Secretary counters with other epidemiologic studies. Resp't's Br. at 31.

For a lengthy discussion of the value of epidemiologic studies in the Vaccine Program, see Tullio v. Sec’y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *5-8 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448, 475 (2020); see also P.M. v. Sec’y of Health & Hum. Servs., No. 16-949V, 2019 WL 5608859, at *24-25 (Fed. Cl. Spec. Mstr. Sep. 24, 2019) (finding that epidemiologic studies weighed against finding the flu vaccine can worsen multiple sclerosis).

Langer-Gould. The primary epidemiologic study from Ms. Mathis’s point of view is Langer-Gould. The investigators explored a potential association between a vaccination and the onset of central nervous system acquired demyelinating syndromes (“CNS ADS”). Langer-Gould at 1507. The researchers used the electronic medical records of the more than 3.5 million members of the Kaiser Permanente Southern California health maintenance organization. Id. By searching various diagnostic codes, the researchers identified people suffering from demyelinating diseases, such as multiple sclerosis, acute disseminated encephalomyelitis, transverse myelitis, and optic neuritis. Id. The researchers matched these examples to controls. Id. The researchers also ascertained when any participants received any vaccination, including the flu vaccination. Id.

The Langer-Gould researchers analyzed the data in various ways, looking for immediate and long-term effects of any vaccination. Id. at 1508. For example, they separately analyzed periods of “14 days, 30 days, 42 days, 90 days, 180 days, 1 year, and 3 years.” Id. The researchers looked at diseases collectively and separately. Id. The researchers also divided the study population by age with a younger group comprised of people younger than 50 years old and an older group comprised of people ages 50 and older. Id.

The Langer-Gould researchers stated that their study had several strengths, such as “a larger sample size, rigorous case-finding methods, inclusion of MS precursors, prospectively recorded symptom onset dates, and complete vaccination records.” Id. at 1512. However, the limitations to their study included the relatively small number of older individuals. Id.

The authors estimated the “matched odds ratio.” Id. at 1508. An odds ratio “expresses in quantitative terms the association between exposure to an agent and a disease.” Michael D. Green, “Reference Guide on Epidemiology,” in Reference Manual on Scientific Evidence (Federal Judicial Center 3d ed.) at 568. “An odds ratio of 1 indicates no association.” David H. Kaye and David A. Freedman, “Reference Guide on Statistics,” in Reference Manual on Scientific Evidence (Federal Judicial Center 3d ed.) at 291.

Langer-Gould and colleagues explained: “we found no long-term association between vaccines and MS or other CNS ADS. We found that younger patients had an increased risk of developing their first symptoms of a CNS ADS up to 30 days following any type of vaccination. However, this association disappeared after 30 days, suggesting that, at most, vaccines are redundant enhancers of preexisting autoimmunity. Our data do not support a causal link between current vaccines and the risk of MS or other CNS ADS.” Id. at 1509-10.

Although Langer-Gould is an exhibit in this case, the experts did not discuss this article extensively. Dr. Chwalisz quoted this article for the proposition that “short-term increase in risk suggests that vaccines may accelerate the transition from subclinical to overt autoimmunity.” Exhibit 17 at 8, quoting Langer-Gould at 1512. Dr. Leist made two points regarding Langer-Gould. Dr. Leist questioned the accuracy of using the earliest diagnostic code for a demyelinating condition as the proxy for the onset of the condition. Exhibit A at 6. To Dr. Leist, problems such as “numbness, fatigue, urinary frequency, stiffness and weakness” could actually mark the onset of the demyelinating disease. Id. Otherwise, Dr. Leist quoted a different portion of the Langer-Gould article in which the authors stated: “there was no increased risk of CNS ADS 30 days after vaccination. This argues against causality because the risk in the vaccinated group should remain elevated regardless of whether the time window between exposure and clinical disease expression is defined as 15 days or 3 years.” Exhibit A at 6, quoting Langer-Gould at 1512. Ms. Mathis did not submit a response from Dr. Chwalisz about Dr. Leist’s comments.

Langer-Gould has been interpreted differently by judicial officers in the Vaccine Program.⁶ Langer-Gould has contributed to a finding that a petitioner failed to establish Althen prong one. Chen v. Sec’y of Health & Hum. Servs., No. 16-634V, 2019 WL 2121208, at *22 (Fed. Cl. Spec. Mstr. Apr. 19, 2019) (petitioner had alleged the flu vaccine caused neuromyelitis optica spectrum disorder). In contrast, another special master found that Langer-Gould supported a 67-year-old petitioner’s claim that vaccines could act as a proinflammatory cofactor. Doles v. Sec’y of Health & Hum. Servs., No. 17-642V, 2021 WL 750416, at *17 (Fed. Cl. Spec. Mstr. Feb. 1, 2021). This finding, however, was overturned by the Court of Federal Claims. Doles v. Sec’y of Health & Hum. Servs., 159 Fed. Cl. 241, 248 (2022) (indicating that although Langer-Gould found

⁶ Neither Ms. Mathis nor the Secretary cited any cases that discussed any epidemiologic studies.

an increased incidence of some neurologic conditions after vaccination in some circumstances, the petitioner did not fit those circumstances).⁷

Langer-Gould warrants analysis by the parties and the experts they retain. For example, if vaccines can cause multiple sclerosis in people aged younger than 50 years old, then why is there not a similar signal among people aged 50 and older? Does something differentiate people younger than 50 from people 50 and older? This analysis would seem especially informative in Ms. Mathis's case because she received the allegedly harmful flu vaccination at age 50. Thus, by the reasoning of the Court of Federal Claims in Doles, 159 Fed. Cl. at 248, the affirmative signal in Langer-Gould for people younger than 50 cannot support Ms. Mathis's claim.

Dr. Leist interposes another potential obstacle impeding a finding that Langer-Gould supports a petitioner's claim. To the extent that Langer-Gould detected an increased incidence of neurologic problems within the first 30 days following a vaccination, why did this increased incidence disappear? See Exhibit A at 6. This potential inconsistency might lessen the reliability of the Langer-Gould finding.

Finally, the language in Langer-Gould, itself, points in different directions. The opening sentence of the concluding paragraph states: "Findings from the present study show no long-term association of vaccines with an increased risk of MS and other CNS ADS." Langer-Gould at 1512. Yet, in the next sentence, as Dr. Chwalisz quoted, the authors also indicate "vaccines (like infections) may accelerate the transition from subclinical to overt autoimmunity in patients with existing disease." Id.

These issues suggest that in the future, parties may wish to retain people trained to comment on Langer-Gould. These people might be epidemiologists, not necessarily neurologists. Any such commentary can await a future case. In the present case, the parties do not rely upon Langer-Gould significantly. As mentioned, the experts' discussion of Langer-Gould amounts to a few sentences. See Exhibit 17 at 8; Exhibit A at 6. Ms. Mathis's brief brings forward Langer-Gould for one paragraph. Pet'r's Br. at 27-28. The Secretary does not cite Langer-

⁷ After a second remand, a different special master indicated that Langer-Gould favored a finding of entitlement. Doles v. Sec'y of Health & Hum. Servs., No. 17-642V, 2023 WL 2750041, at *24 n.14 (Fed. Cl. Spec. Mstr. Apr. 3, 2023), mot. for rev. filed (Apr. 14, 2023). The pending motion for review raises questions involving Langer-Gould.

Gould at all. Thus, due to the small weight placed upon Langer-Gould by the parties, more discussion is not warranted.

Mealy. Ms. Mathis also cites a study by Mealy. Pet'r's Br. at 29. Mealy and others evaluated whether vaccines were associated with an increased risk of relapse in a demyelinating condition known as neuromyelitis optica. Neuromyelitis optica differs from multiple sclerosis. As such, Mealy warrants less weight than studies involving multiple sclerosis. Furthermore, no decisions with a substantive analysis of Mealy were identified.

Karussis. The final article Ms. Mathis cites in the context of epidemiology is by Karussis. Pet'r's Br. at 28. The researchers searched PubMed for articles in which a vaccination was noted to precede the onset of a demyelinating disease between 1979 and 2013. Over the course of these 34 years, the researchers identified 71 examples. Karussis proposed that the mechanism by which a vaccination might bring about a demyelinating disease might be the autoimmune syndrome induced by adjuvants ("ASIA") or molecular mimicry. Karussis ultimately concluded that the risk of a vaccine causing a demyelinating disease "although non-negligible, is relatively low." Karussis at 221.

For the proposition that a vaccine can cause (or aggravate) multiple sclerosis, Karussis merits little weight. Essentially, the authors gathered multiple case reports to form a case series. See Doles, 2023 WL 2750041, at *23 (recognizing Karussis as a type of case report). In this case series, the authors identified approximately two examples per year of a demyelinating condition appearing after a vaccination. The authors did not present any information about how many vaccinations are given per year, nor did they present any information about how many demyelinating diseases are diagnosed each year. In addition, Karussis did not show any information about controls. Furthermore, Karussis did not identify multiple sclerosis as a demyelinating disease potentially linked to a vaccination. See Porch v. Sec'y of Health & Hum. Servs., No. 17-1802V, 2023 WL 21875 at *7, 22 (Fed. Cl. Spec. Mstr. Dec. 8, 2022).

Based at least in part on these deficits, the Federal Circuit stated in a non-precedential opinion that Karussis is not "a study showing causation." Orloski v. Sec'y of Health & Hum. Servs., 839 Fed. App'x 538, 542 (Fed. Cir. 2021).

Those three articles are the ones Ms. Mathis cites. The Secretary brings forward other articles.

Mokhtarian. The earliest article the Secretary cites was published in 1997. This study involved approximately 20 people. The authors concluded that their study “suggests that influenza vaccine can be administered to MS patients with EDSS of less than 6.5 without exacerbation of disease.” Mokhtarian at 246-47. (A Kurtzke Extended Disability Status Score of less than 6.5 means that the person is ambulatory with no more than a unilateral aid. Id. at 243-44.) This article appears not to have been cited by any judicial officer in the Vaccine Program.

Miller. This article, which was published in 1997, reported the results of an experiment involving 104 patients with relapsing-remitting multiple sclerosis. These patients randomly received either a flu vaccine or a placebo. Miller at 312. The researchers followed the participants for six months to see whether anyone’s multiple sclerosis worsened. In this period, there “was no significant difference in the numbers of patients who worsened.” Id. at 313. “The mean time of onset of relapse after flu vaccine (91.5 days) exceeded that for placebo patients (55.3 days), further substantiating the lack of association between flu vaccine and MS exacerbations.” Id.

Because of the placebo in the experiments, the results in Miller were emphasized by the (undersigned) special master in W.C. v. Sec’y of Health & Hum. Servs., No. 07-456V, 2011 WL 4537877, at *15 (Fed. Cl. Spec. Mstr. Feb. 22, 2011). Upon a motion for review, a judge from the Court of Federal Claims found the special master’s overall finding that the evidence regarding whether a flu vaccine might significantly aggravate multiple sclerosis to be “closely balanced.” W.C. v. Sec’y of Health & Hum. Servs., 100 Fed. Cl. 440, 456 (2011). The Court declined to find the special master’s overall determination that the petitioner had not established that a flu vaccination can aggravate multiple sclerosis arbitrary or capricious. Id. The Federal Circuit also ruled that Miller and other epidemiologic studies supported the opinion of the Secretary’s expert that a causal link between a flu vaccination and a relapse of multiple sclerosis was “extremely unlikely.” W.C. v. Sec’y of Health & Hum. Servs., 704 F.3d 1352, 1361 (Fed. Cir. 2013).

Mailand. In 2017, a group of researchers investigated whether vaccines affected the risk of developing multiple sclerosis and whether vaccines affected the risk of having a multiple sclerosis relapse. The researchers did so by reviewing literature systematically. Mokhtarian and Miller were included among the 20 articles on the flu vaccine. Of the 14 studies about whether the flu vaccine might cause multiple sclerosis to worsen, 13 studies “found no increased risk of relapse following vaccination against seasonal influenza or H1N1.” Mailand at 1036.

Special masters have tended to view Mailand as undermining a contention that vaccinations can cause (or aggravate) multiple sclerosis. Walker, 2022 WL 11141104, at *5 (finding that petitioner did not establish a flu vaccine can aggravate multiple sclerosis); P.M., 2019 WL 5608859, at *22 (finding ample evidence including Mailand contrary to the proposition that a flu vaccine can aggravate multiple sclerosis); Maciel v. Sec'y of Health & Hum. Servs., No. 15-362V, 2018 WL 6259230, at *27-28 (Fed. Cl. Spec. Mstr. Oct. 12, 2018) (finding that petitioners did not establish a human papillomavirus vaccine can cause multiple sclerosis). But see Porch, 2023 WL 21875, at *13 (the Secretary's expert recognizing that the authors might have been biased).

Farez. Operating through a designated committee, the American Academy of Neurologists in 2019 issued a series of guidelines for how neurologists might respond to questions about how vaccinations might affect people with multiple sclerosis. To form their guidelines, these authors conducted a systemic literature review and assessed the value of the literature. They advised: "Clinicians should recommend that patients with MS receive the influenza vaccination annually." Farez at 584. The Farez group also found that the "Data were insufficient to support or refute an association between development of MS and a history of vaccination for ... influenza." Id. at 586.

Overall Assessment of Epidemiologic Studies. Taken together, the epidemiologic evidence weighs against finding that the flu vaccine can cause (or aggravate) multiple sclerosis. Decisions that meaningfully analyze epidemiology have tended to reach similar results. See Walker, 2022 WL 11141194, at *5; P.M., 2019 WL 5608859, at *22 (noting "ample evidence" against finding a flu vaccine exacerbates multiple sclerosis).

One decision that reached a contrary result did so, in part, because the epidemiology was viewed as not being in complete agreement. Doles, 2021 WL 750416, at *18 n.14. However, the persuasive value of this ruling is uncertain for a few reasons. First, this assessment was largely based upon Karussis and Karussis is not actually an epidemiologic study. Second, Doles did not discuss the Federal Circuit's analysis of Karussis in its non-precedential opinion Orloski, 839 F. App'x at 542. Third, the Court of Federal Claims vacated the Doles decision, 159 Fed. Cl. at 248, although the opinion of the Court of Federal Claims might be subject to further appellate review.

To be sure, the epidemiologic evidence in this record is not of such quality or quantity that the issue is open and shut. Some of the epidemiologic studies may contain flaws that lessen their value. However, as pointed out in Porch, a

conclusion that some of respondent's epidemiologic evidence is not valuable does not necessarily strengthen petitioner's case. 2023 WL 21875 at *24. A petitioner can receive compensation even in the absence of epidemiologic studies. Thus, the theories Ms. Mathis advances to explain how a flu vaccine can significantly aggravate multiple sclerosis are considered next.

B. Individual Theories

Ms. Mathis proposes three theories by which a flu vaccine can harm someone with multiple sclerosis. These are: molecular mimicry, bystander activation, and instigation of complement. Pet'r's Br. at 30-35.

1. Molecular Mimicry

Because special masters are often called upon to evaluate the persuasiveness of the theory of molecular mimicry, the Court of Federal Claims and the Court of Appeals for the Federal Circuit have considered molecular mimicry in their appellate role. In December 2019, the undersigned identified the leading precedents as W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352 (Fed. Cir. 2013), and Caves v. Sec'y of Dep't. of Health & Hum. Servs., 100 Fed. Cl. 119 (2011), aff'd sub nom., 463 F. App'x 932 (Fed. Cir. 2012). Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *12-14 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448 (2020). While Tullio describes those cases in more detail, their essence appears to be that although molecular mimicry is accepted in some contexts, special masters may properly require some empirical evidence to show that a particular vaccine can cause a particular disease.

In the next approximately three years, appellate authorities reviewing decisions involving molecular mimicry have generally endorsed the approach of looking for some evidence that persuasively shows that a portion of a vaccine resembles a portion of human tissue, which contributes to causing the disease, and that the immune system will respond to the relevant amino acid sequence.⁸ Chronologically, the list of more recent appellate cases begins with the opinion in Tullio, which denied the motion for review. 149 Fed. Cl. 448, 467-68 (2020).

⁸ The term "homology" is used when discussing molecular mimicry. "Homology" is defined as "the quality of being homologous; the morphological identity of corresponding parts; structural similarity due to descent from a common form." *Dorland's* at 868.

Another example in which the Court of Federal Claims held that the special master did not elevate the petitioner's burden of proof in the context of evaluating the theory of molecular mimicry is Morgan v. Sec'y of Health & Hum. Servs., 148 Fed. Cl. 454, 476-77 (2020), aff'd in non-precedential opinion, 850 F. App'x 775 (Fed. Cir. 2021). In Morgan, the Chief Special Master found that petitioner had not presented persuasive evidence about a relevant antibody. Id. at 477. The Chief Special Master also noted that the articles about the relevant disease do not list the wild flu virus as potentially causing the disease. Id. When examining this analysis, the Court of Federal Claims concluded: "the Chief Special Master did not raise the burden of causation in this case; petitioner simply failed to meet it." Id.

The Federal Circuit also evaluated the Chief Special Master's approach in Morgan. The Federal Circuit concluded: "We discern no error in the special master's causation analysis." 850 F. App'x 775, 784 (Fed. Cir. 2021).

Most other recent appellate cases follow this path. See, e.g., Duncan v. Sec'y of Health & Hum. Servs., 153 Fed. Cl. 642, 661 (2021) (finding the special master did not err in rejecting a bare assertion of molecular mimicry); Caredio v. Sec'y of Health & Hum. Servs., No. 17-79V, 2021 WL 6058835, at *11 (Fed. Cl. Dec. 3, 2021) (indicating that a special master did not err in requiring more than homology and citing Tullio); Yalacki v. Sec'y of Health & Hum. Servs., 146 Fed. Cl. 80, 91-92 (2019) (ruling that special master did not err in looking for reliable evidence to support molecular mimicry as a theory); but see Patton v. Sec'y of Health & Hum. Servs., 157 Fed. Cl. 159, 169 (2021) (finding that a special master erred in requiring petitioner submit a study to establish medical theory causally connecting flu vaccine to brachial neuritis).

Under this method of analysis, the evidence Ms. Mathis presents falls short of her burden. Dr. Chwalisz cites a series of articles purporting to link substances other than the flu vaccine to neurologic conditions that differ from multiple sclerosis. Exhibit 17 at 5-6. But, Dr. Chwalisz provides no persuasive reason for extending these other substances, such as the Zika virus, to the flu vaccine, and provides no persuasive reason for likening multiple sclerosis to other diseases. Dr. Chwalisz also does not propose any homology between the flu vaccine and a body part implicated in the pathogenesis of multiple sclerosis. Ms. Mathis's brief is similarly conclusory on this topic. See Pet'r's Br. at 30.

2. Bystander Activation

Dr. Chwalisz's discussion of bystander activation consists of one paragraph containing two sentences and citing two articles. Exhibit 17 at 6. Ms. Mathis's brief matches this level of detail. See Pet'r's Br. at 31.

When an expert presents bystander activation without much explanation, special masters may reject this theory. See Temes v. Sec'y of Health & Hum. Servs., 151 Fed. Cl. 448, 461-62 (2020), Shapiro v. Sec'y of Health & Hum. Servs., 105 Fed. Cl. 353, 359 (2012), aff'd without op., 503 F. App'x 952 (Fed. Cir. 2013). While Dr. Chwalisz and the articles he cites have been considered, they are not persuasive in this context.

3. Instigation of Complement

The third and final theory involves complement. The presentation of this theory is lengthier. See Exhibit 17 at 6-7; Pet'r's Br. at 31-34. While longer, the theory based on complement is not any more persuasive. The two key articles are both written by Ingram. The undersigned previously found that these articles do not support a finding that complement instigated by a vaccine could contribute to the onset of multiple sclerosis. Walker, 2022 WL 11141194, at *5.

C. **Summary**

Ms. Mathis has not met her burden to explain a way by which the flu vaccine might cause a previously asymptomatic case of multiple sclerosis to become manifest.⁹ The epidemiology tends to weigh against such a finding. More significantly, the three theories Ms. Mathis proposed were not sufficiently developed.

Because Ms. Mathis's case is resolved based upon the fourth Loving prong (equivalent to the first Althen prong), further evaluation of the remaining prongs is not necessary. When special masters can resolve a case based upon one issue, they do not necessarily need to address all issues. See, e.g., Hibbard v. Sec'y of Health & Hum. Servs., 698 F.3d 1355, 1365 (Fed. Cir. 2012); Holmes v. Sec'y of

⁹ The description of Ms. Mathis's multiple sclerosis as "previously asymptomatic" accepts for sake of argument the way Dr. Chwalisz has postured her case. Exhibit 17 at 10. Dr. Leist disputes the assertion that Ms. Mathis had not demonstrated any symptoms of multiple sclerosis before the vaccination. Exhibit A at 7. Resolving this issue is not necessary.

Health & Hum. Servs., 115 Fed. Cl. 469, 488 (2014); Vaughan v. Sec’y of Health & Hum. Servs., 107 Fed. Cl. 212, 222 (2012).

V. Conclusion

The diagnosis of multiple sclerosis approximately two months after the flu vaccination may have led Ms. Mathis to believe that the flu vaccine contributed to her development of this disease. As someone living with a chronic condition, Ms. Mathis merits sympathy. However, her efforts to present a legally persuasive claim faltered. As explained above, Ms. Mathis has not shown how the flu vaccine might contribute to multiple sclerosis. Accordingly, she is not entitled to compensation.

The Clerk’s Office is instructed to enter judgment in accordance with this decision unless a motion for review is filed. Information about filing a motion for review, including the deadline, can be found in the Vaccine Rules, available through the Court’s website.

IT IS SO ORDERED.

s/Christian J. Moran
Christian J. Moran
Special Master

Appendix: List of Medical Articles Cited¹

1. Mauricio F. Farez et al., Practice guideline update summary: Vaccine-preventable infections and immunization in multiple sclerosis. 93 NEUROLOGY 584 (2019); filed as Exhibit 27.
2. G. Ingram et al., Complement in multiple sclerosis: its role in disease and potential as a biomarker. 155 CLIN. EXP. IMMUNOL. 128 (2009); filed as Exhibit 31.
3. G. Ingram et al., Complement activation in multiple sclerosis plaques: an immunohistochemical analysis. 2 ACTA NEUROPATHOLOGICA COMMUNICATIONS 53 (2014); filed as Exhibit 32.
4. Dimitrios Karussis & Panayiota Petrou, The spectrum of post-vaccination inflammatory CNS demyelinating syndromes. 13 AUTOIMMUN. REV. 215 (2014); filed as Exhibit 33.
5. Annette Langer-Gould et al., Vaccines and the risk of multiple sclerosis and other central nervous system demyelinating diseases. 71 JAMA NEUROL. 1506 (2014); filed as Exhibit 37.
6. Mia Topsøe Mailand & Jette Lautrup Frederiksen, Vaccines and multiple sclerosis: a systematic review. 264 J. NEUROL. 1035 (2017); filed as Exhibit A-1.
7. Maureen A. Mealy et al., Vaccines and the association with relapses in patients with neuromyelitis optica spectrum disorder. 23 MULT. SCLER. RELAT. DISORD. 78 (2018); filed as Exhibit 40.
8. A. E. Miller et al., A multicenter, randomized, double-blind, placebo-controlled trial of influenza immunization in multiple sclerosis. 48 NEUROLOGY 312 (1997); filed as Exhibit 41.
9. F. Mokhtarian et al., Influenza virus vaccination of patients with multiple sclerosis. 3 MULT. SCLER. 243 (1997); filed as Exhibit 43.

¹ All articles have been considered.